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EXAMINER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ROLAND KREUTZER and STEFAN LIMMER¹

Appeal 2014-005642
Application 13/753,438
Technology Center 1600

Before FRANCISCO C. PRATS, RICHARD J. SMITH, and TAWEN
CHANG, *Administrative Patent Judges*.

SMITH, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to an oligoribonucleotide of double-stranded structure (dsRNA). We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

¹ According to Appellants, the real party in interest is Alnylam Pharmaceuticals, Inc. (Appeal Br. 2.)

STATEMENT OF THE CASE

Claims on Appeal

Claims 1–15 are on appeal.² (Claims Appendix, Appeal Br. 14–15.)

Claim 1 (emphasis added) and claim 9 are illustrative and read as follows:

1. An oligoribonucleotide of double-stranded structure (dsRNA) for introduction into a mammalian cell and for inhibiting the expression of a given target gene in a mammalian cell, *wherein an amount of the dsRNA introduced into the mammalian cell is less than an amount of RNA transcript of the target gene in the mammalian cell*, the dsRNA having 15 to 49 base pairs and having a complementary region I that is incorporated in the dsRNA, and wherein the complementary region I has not more than 49 nucleotide pairs.

9. The dsRNA of claim 1, wherein the dsRNA is capable of inhibiting expression at a concentration of the dsRNA that is lower by one order of magnitude than a concentration required for a corresponding single-stranded oligoribonucleotide to inhibit expression.

Examiner's Rejections

1. Claims 1–9, 12, and 13 stand rejected on the ground of nonstatutory obviousness-type double patenting over claims 1 and 2 of U.S. Patent No. 7,198,814³ in view of Crooke⁴ and Wengel.⁵ (Ans. 2.)

2. Claims 1, 7, and 9–11 stand rejected on the ground of nonstatutory obviousness-type double patenting over claims 11 and 26 of U.S. Patent No. 7,745,418.⁶ (*Id.* at 3.)

² Claims 16–18 are withdrawn from consideration as being directed to a non-elected invention. (Final Act. dated Sept. 13, 2013, at 2.)

³ Endo et al., US 7,198,814 B2, issued Apr. 3, 2007.

⁴ Crooke, US 6,107,094, issued Aug. 22, 2000 (“Crooke”).

⁵ Wengel, US 2003/0134808 A1, published July 17, 2003 (“Wengel”).

⁶ John et al., US 7,745,418 B2, issued June 29, 2010.

3. Claims 1, 7–9, 12, and 13 stand rejected on the ground of nonstatutory obviousness-type double patenting over claims 1 and 3 of U.S. Patent No. 7,829,693.⁷ (*Id.*)
4. Claims 1 and 7–12 stand rejected on the ground of nonstatutory obviousness-type double patenting over claims 1, 5–8, 13, 17–19, 22, 23, 29, and 30 of U.S. Patent No. 7,994,309.⁸ (*Id.*)
5. Claims 1–9, 12, and 13 stand rejected on the ground of nonstatutory obviousness-type double patenting over claims 1–24 of U.S. Patent No. 8,101,742.⁹ (*Id.* at 3–4.)
6. Claims 1–13 stand rejected on the ground of nonstatutory obviousness-type double patenting over claims 1–22 of U.S. Patent No. 8,114,981.¹⁰ (*Id.* at 4.)
7. Claims 1–9, 12, and 13 stand rejected on the ground of nonstatutory obviousness-type double patenting over claims 1–6 and 9–16 of U.S. Patent No. 8,183,362.¹¹ (*Id.* at 4–5.)
8. Claims 1, 7–9, 12, and 13 stand rejected on the ground of nonstatutory obviousness-type double patenting over claims 1–17 of U.S. Patent No. 8,202,980.¹² (*Id.* at 5.)

⁷ Kreutzer et al., US 7,829,693 B2, issued Nov. 9, 2010.

⁸ Kreutzer et al., US 7,994,309 B2, issued Aug. 9, 2011.

⁹ Kreutzer et al., US 8,101,742 B2, issued Jan. 24, 2012.

¹⁰ Kreutzer et al., US 8,114,981 B2, issued Feb. 14, 2012.

¹¹ Kreutzer et al., US 8,183,362 B2, issued May 22, 2012.

¹² Kreutzer et al., US 8,202,980 B2, issued June 19, 2012.

9. Claims 1 and 7–12 stand rejected on the ground of nonstatutory obviousness-type double patenting over claims 1, 5–8, 14, 18–20, 30, and 31 of U.S. Patent No. 8,273,870.¹³ (*Id.* at 5–6.)
10. Claims 1, 7, and 9–11 stand rejected on the ground of nonstatutory obviousness-type double patenting over claims 9 and 22 of U.S. Patent No. 8,273,868.¹⁴ (*Id.* at 6.)
11. Claim 14 stands rejected under 35 U.S.C. § 112(b) or 35 U.S.C. § 112 (pre-AIA), second paragraph, as indefinite. (*Id.*)
12. Claims 1–5, 7–9, 12, 13, and 15 stand rejected under 35 U.S.C. § 102(e) as anticipated by Crooke. (*Id.* at 6–8.)
13. Claims 1–13 and 15 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Crooke, Sridhar,¹⁵ and Wengel. (*Id.* at 8–9.)

FINDINGS OF FACT

We adopt as our own the Examiner’s findings and analysis concerning the scope and content of the prior art. The following findings are included for emphasis and reference convenience.

FF 1. The Examiner finds that Crooke teaches “oligomeric compounds that bind to a target RNA strand and are substrates for dsRNase enzymes,” and that the “oligomeric compounds include oligoribonucleotides and other oligomeric compounds having a linear sequence of linked ribonucleoside subunits incorporated therein.” (Ans. 6, citing Crooke col. 12.)

¹³ Kreutzer et al., US 8,273,870 B2, issued Sept. 25, 2012.

¹⁴ John et al., US 8,273,868 B2, issued Sept. 25, 2012.

¹⁵ Sridhar et al., US 5,739,271, issued Apr. 14, 1998 (“Sridhar”).

FF 2. Crooke teaches that the compounds of the invention are “useful for therapeutics, diagnostics and as research reagents.” (Crooke col. 1, ll. 24–27.)

FF 3. Crooke teaches that “[i]t is more preferred that the oligoribonucleotides and oligoribonucleosides of the present invention comprise from about 15 to about 25 nucleoside subunits.” (Crooke col. 14, ll. 13–16.)

FF 4. The Examiner finds that

While Crooke does not explicitly disclose use of his compounds to inhibit gene expression or that these compounds are capable of inhibiting expression at a concentration one order of magnitude lower than a single stranded compound, because Crooke discloses compounds satisfying the structural limitations of the claims, these characteristics are assumed in the absence of factual evidence to the contrary to be inherent to the structure.

(Ans. 7–8.)

FF 5. The Examiner finds that “use of liposomes as a vehicle for delivering nucleic acids to cells was well known at the time the invention was made” and that “liposomes are useful for intracellular delivery of oligonucleotides for diagnostic purposes.” (Ans. 9, citing Sridhar Abstract; col. 1, l. 53–col. 2, l. 13.)

DISCUSSION

We adopt and agree with the Examiner’s findings, analysis, and conclusions set forth in the Final Action (Final Act. 3–13) and Examiner’s Answer (Ans. 2–14). The rejections are affirmed, and Appellants’ arguments are addressed below.

Rejection Nos. 1–11

Appellants do not contest the rejections for obviousness-type double patenting (Nos. 1–10) or the rejection for indefiniteness (No. 11).

Accordingly, those rejections are affirmed. *See* 37 C.F.R. § 41.37(c)(1)(iv); *Hyatt v. Dudas*, 551 F.3d 1307, 1314 (Fed. Cir. 2008).

Rejection No. 12—Anticipation

Issue

Whether a preponderance of evidence of record supports the Examiner’s finding of anticipation under 35 U.S.C. § 102(e).

Principles of Law

A claim is anticipated if a prior art reference discloses every limitation of the claimed invention, either explicitly or inherently. *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997). In considering the disclosure of a reference for anticipation, “it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom.” *In re Preda*, 401 F.2d 825, 826 (CCPA 1968). “Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates.” *MEHL/Biophile Int’l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999).

Analysis

Appellants argue that neither claim 1 nor claim 9 are anticipated by Crooke. (Appeal Br. 3–6; Reply Br. 2–5.)

Claim 1

Appellants argue that Crooke does not teach each and every limitation of the claimed invention because “Crooke does not disclose a dsRNA for

introduction into a mammalian cell and for inhibiting the expression of a given target gene in the cell, *wherein the amount of dsRNA is less than an amount of RNA transcript of the target gene in the cell.*” (Appeal Br. 4.)

Appellants argue further that “an amount of Crooke’s RNA duplex substrate is not disclosed in Crooke at all.” (*Id.*)

Appellants also challenge the finding that the italicized *wherein* clause in claim 1 relates to an intended use of the claimed compound, arguing that “the amount of dsRNA is not an intended use of the dsRNA . . . but refers to an amount or a physical limitation associated with the claimed dsRNA.” (*Id.* at 5.) Appellants argue further that, while claim 1 “recites ‘introduced into’ language that sounds like a use,” the “claim language merely specifies the conditions by which the amount (physical aspect) is measured.” (*Id.*)

We are not persuaded. “[T]he patentability of apparatus or composition claims depends on the claimed structure, not on the use or purpose of that structure.” *Catalina Mktg. Int’l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 809 (Fed. Cir. 2002). Appellants’ claim 1 is to a composition of matter, *i.e.*, an oligoribonucleotide of double-stranded structure (dsRNA). (Appeal Br. 14.) Moreover, the claim language “*wherein an amount of the dsRNA introduced into the mammalian cell is less than an amount of RNA transcript of the target gene in the mammalian cell*” refers to the intended use of the dsRNA; namely, “for introduction into a mammalian cell and for inhibiting the expression of a given target gene in a mammalian cell.” (*Id.*) That the italicized phrase fails to recite a structural limitation is further evidenced by the fact that the recited “amount” of dsRNA depends on the amount of RNA transcript, *i.e.*, depending on the use of the claimed dsRNA. (*Id.*)

We acknowledge, but are unpersuaded by, Appellants’ analogies to the size of a widget or amount of a liquid (Appeal Br. 5), and Appellants’ arguments based on *In re Lemin*, 326 F.2d 437 (CCPA 1964) and *In re Wiggins*, 397 F.2d 356 (CCPA 1968) (Reply Br. 2–5). The “amount of the dsRNA” recited in claim 1 relates to an intended use and does not become a structural limitation simply because of the word “amount.”¹⁶

We agree with the Examiner’s finding that Crooke discloses each and every limitation of claim 1. Moreover, the argument that Crooke does not disclose a dsRNA for introduction into a mammalian cell or an amount of its RNA duplex structure (*i.e.*, use of dsRNA for the same use as recited in claim 1) does not overcome the anticipation finding. *See Schreiber*, 128 F.3d at 1475–77 (claim to a dispensing top for popcorn anticipated by patent disclosing a spout useful for dispensing oil from an oil can).

Claim 9

Appellants argue that Crooke does not anticipate dependent claim 9 because “Crooke does not satisfy the structural limitations of the claims” and, therefore, “a dsRNA capable of inhibiting expression at a particular concentration is not inherent in Crooke.” (Appeal Br. 6.) We are not persuaded. The contention that the claimed dsRNA is “capable” of inhibiting expression does not impart patentable weight since the structure is already known. *See Schreiber*, 128 F.3d at 1477. And because Crooke discloses the claimed structure, Crooke’s dsRNA will necessarily have the

¹⁶ We do not agree with Appellants’ contention, based on *Lemin* and *Wiggins*, that an amount recited in a composition claim is necessarily a “physical limitation.” (Reply Br. 2–5.) *See, e.g., Syntex (U.S.A.) LLC v. Apotex, Inc.*, 407 F.3d 1371, 1378 (Fed. Cir. 2005) (construing the term “in a stabilizing amount” in a drug formulation claim as not a limitation).

same inherent property as recited in claim 9. (FF 4.) *See MEHL/Biophile*, 192 F.3d at 1365; *In re Pearson*, 494 F.2d 1399, 1403 (Fed. Cir. 1974) (“These terms merely set forth the intended use for, or a property inherent in, an otherwise old composition.”).

Conclusion

A preponderance of evidence of record supports the Examiner’s finding that claims 1 and 9 are anticipated under 35 U.S.C. § 102(e). Claims 2–5, 7, 8, 12, 13, and 15 were not argued separately and fall with claim 1.

Rejection No. 13—Obviousness

Issue

Whether a preponderance of evidence of record supports the Examiner’s conclusion of obviousness under 35 U.S.C. § 103(a).

Analysis

Appellants contest the obviousness rejection with respect to claims 1, 10, 11, and 15. (Appeal Br. 6–12; Reply Br. 5–7.) However, “anticipation is the epitome of obviousness.” *In re McDaniel*, 293 F.3d 1379, 1385 (Fed. Cir. 2002) (citations omitted). Accordingly, as to claims 1 and 15 that are anticipated by Crooke, we affirm their rejection for obviousness as well.

Claims argued by Appellants that were not subject to the anticipation rejection include claim 10 (dependent on claim 1) that recites “wherein the dsRNA is enclosed by a micellar structure,” and claim 11 (dependent on claim 10) that recites “wherein the micellar structure comprises a liposome.” (Appeal Br. 15.) The Examiner cites Sridhar for teaching liposomes as a vehicle for delivering nucleic acids to cells (FF 5), and concludes that “[b]ecause those of ordinary skill in the art were aware that liposomes are a convenient delivery vehicle for nucleic acids, it would have been obvious to

incorporate artificial nuclease substrates into liposomes in order to obtain the advantages of liposome encapsulation.” (Ans. 9.)

Claim 10

Appellants argue that “Crooke did not present or express a desire to present RNA duplexes into a cellular system” and, thus, “[o]ne skilled in the art would not put the RNA duplexes of Crooke into liposomes, since there is no reason or motivation to deliver Crooke’s RNA duplexes into cells.” (Appeal Br. 9; *see also* Reply Br. 5–7.) Appellants also argue that “Crooke only produced RNA duplexes to test whether the duplexes would be cleaved in the presence of rat liver extracts” (Appeal Br. 9), and that “the skilled artisan would have understood that it was necessary to introduce only a single-stranded structure into the cell to cause degradation of the target mRNA” (*Id.* at 10).

We are not persuaded. A prior art reference may be read for all that it teaches, including uses beyond its primary purpose. *In re Mouttet*, 686 F.3d 1322, 1331 (Fed. Cir. 2012). Moreover, “[i]n determining whether the subject matter of a patent claim is obvious, neither the particular motivation nor the avowed purpose of the patentee controls,” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 419 (2007), and “[o]ne of ordinary skill in the art need not see the identical problem addressed in a prior art reference to be motivated to apply its teachings” *Cross Med. Prods., Inc. v. Medtronic Sofamor Danek, Inc.* 424 F.3d 1293, 1323 (Fed. Cir. 2005). Furthermore, evaluating suggestion or motivation in an obviousness analysis “not only permits, but *requires*, consideration of common knowledge.” *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1367 (Fed. Cir. 2006).

Accordingly, we do not find that Crooke's teachings are so limited as argued by Appellants.¹⁷ Here, Crooke teaches that its compounds "are useful for therapeutics, diagnostics and as research reagents" (FF 2) and Appellants concede that "Crooke is not limited only to extracellular uses" (Appeal Br. 9).

Given that Crooke's compounds are useful for diagnostics (FF 2), and Sridhar's teaching that liposomes "can effectively be used for the intracellular delivery of biomolecules for . . . diagnostic purposes" (Sridhar Abstract), which was common knowledge in the art (FF 5), we find the claimed invention to be the "predictable use of prior art elements according to their established functions." *KSR*, 550 U.S. at 417. Moreover, a person of ordinary skill in the art would have been motivated to combine the dsRNA of Crooke with the liposomes (micellar structures) of Sridhar "in order to obtain the advantages of liposome encapsulation." (Ans. 9.)

Claim 11

Appellants repeat the arguments advanced in connection with claim 10, and they are unpersuasive as to claim 11 for the reasons set forth above.

Conclusion of Law

A preponderance of evidence of record supports the Examiner's conclusion that claims 1, 10, 11, and 15 are obvious under 35 U.S.C. § 103(a). Claims 2–9, 12, and 13 were not argued separately and fall with claim 1.

¹⁷ We also acknowledge, but are unpersuaded by, Appellants' argument that Crooke "teaches away." (Appeal Br. 8.) Crooke does not teach away because it does not criticize, discredit, or otherwise discourage the claimed invention. See *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004).

Appeal 2014-005642
Application 13/753,438

SUMMARY

We affirm the rejections of all claims on appeal.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED